

Appl. No. 09/724,369  
Amdt. dated December 7, 2004  
Reply to Restriction/Election Requirement of July 8, 2004

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**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings of claims in the application:

**Listing of Claims:**

Claims 1-55. (Canceled)

56. (Currently Amended) An isolated nucleic acid, comprising a sequence of nucleotides that encodes a  $\beta$ -secretase protein that is at least 95% identical to a protein selected from the group consisting of SEQ ID NO: 66 [22-501], SEQ ID NO: 43[46-501], SEQ ID NO: 57 [1-419], SEQ ID NO: 74 [22-452], SEQ ID NO: 58 46-452], SEQ ID NO: 59 [1-452], SEQ ID NO: 60 [1-420], SEQ ID NO: 67 [58-501], SEQ ID NO: 68 [58-452], SEQ ID NO: 69 [63-501], SEQ ID NO: 70 [63-452], SEQ ID NO: 75 [63-423], and SEQ ID NO: 71 [46-419], or a complementary sequence of any of such nucleotides, and specifically excluding a nucleic acid encoding a protein having the sequence SEQ ID NO: 2 [1-501].

57. (Currently Amended) The isolated nucleic acid of claim 56, wherein said sequence of nucleotides encodes a protease having an amino acid sequence SEQ ID NO: 58 [46-452]

58. (Currently Amended) 58. The isolated nucleic acid of claim 56, wherein said sequence of nucleotides encodes a protease having the sequence SEQ ID NO: 43 [46-501].

59. (Currently Amended) The isolated nucleic acid of claim 56, wherein said sequence of nucleotides encodes a protease having the sequence SEQ ID NO: 66 [22-501].

60. (Currently Amended) The isolated nucleic acid of claim 56, wherein said sequence of nucleotides encodes a protease having the sequence SEQ ID NO: 74 [22-452].

61. (Original) A expression vector, comprising  
the isolated nucleic acid of claim 56, and

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operably linked to said nucleic acid, regulatory sequences effective for expression of the nucleic acid in a selected host cell.

62. (Original) The recombinant expression vector of claim 61, wherein said vector is suitable for transfection of a bacterial cell.

63. (Original) A heterologous cell transfected with the vector of claim 61, wherein said cell expresses a biologically active  $\beta$ -secretase.

64. (Original) The cell of claim 63, wherein said cell is a eukaryotic cell.

65. (Original) The cell of claim 63, wherein said cell is a bacterial cell.

66. (Original) The cell of claim 63, wherein said cell is an insect cell.

67. (Original) The cell of claim 63, wherein said cell is a yeast cell.

68. (Original) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell according to claim 63 under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

69. (Original) The method of claim 68, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

70. (Currently Amended) The method of claim 69, wherein said inhibitor molecule is SEQ ID NO: 72 [~~P10-P4'staD~~  $\rightarrow$  V].

71. (Original) The method of claim 68, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

72. (Original) The method of claim 71, wherein said antibody is according to claim 55.

73. (Original) A heterologous cell, comprising

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(i) a nucleic acid molecule encoding an active  $\beta$ -secretase protein according to claim 55;

(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and

(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

74. (Original) The cell of claim 73, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

75. (Original) The cell of claim 73, wherein both said nucleic acids encoding said  $\beta$ -secretase protein encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

76. (Original) The cell of claim 73, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of MBP-C125wt, MBP-C125sw, APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

77. (Original) The cell of claim 76, wherein said  $\beta$ -secretase-cleavable fragment has a sequence selected from the group consisting of SEQ ID NO: 82, SEQ ID NO: 83, SEQ ID NO: 84, SEQ ID NO: 85, SEQ ID NO: 86, SEQ ID NO: 87, SEQ ID NO: 88, SEQ ID NO: 89, SEQ ID NO: 90, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 93, SEQ ID NO: 94, SEQ ID NO: 95, and SEQ ID NO: 96.

Claims 78-131 (Canceled)